

MOLECULAR EVOLUTION AND EPIDEMIOLOGY OF DENGUE-4 VIRUSES IN BANGKOK, THAILAND

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Fifty-three dengue-4 (DEN-4) virus isolates from children in Bangkok, Thailand, admitted with varying severity of dengue [dengue fever/dengue hemorrhagic fever/dengue shock syndrome (DF/DHF/DSS)] from 1976 to 2002 were selected to sequence the envelope (E) gene for identifying specific sequence patterns which may correlate with disease severity and for assessing potential trends in molecular evolution and epidemiology of circulating DEN-4 viruses within Bangkok. Phylogenetic analysis of these isolates revealed that the majority collected in the past 27 years comprised genotype I (47 cases), 5 of the 6 more recent isolates comprised a genotype never previously described. This newly discovered genotype was associated with DF (2 cases) and DHF/DSS (3 cases). No specific sequence differences were identified between the DF and DHF/DSS isolates, suggesting that the E gene alone did not determine disease severity. The phylogenetic tree revealed that genotype I of DEN-4 virus circulating in Bangkok appears to have become extinct beyond 1999 and has been replaced by new lineages that emerged in 1998 and evolved locally, rather than having been introduced. However, it remains unclear and requires further study as to whether this replacement represents a selection event, so that strains differ in fitness, or a random population bottleneck. One case of the genotype IIA appears to have been introduced in 2000 from neighboring Malaysia or Indonesia where this genotype is known to circulate. However, it appears that this genotype could not be sustained. Sequencing of the entire virus genome of selected specimens is underway to ascertain the molecular basis to any differences in fitness among strains.

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NITRIC OXIDE RADICAL: FROM AN *IN VITRO* EXPERIMENT TO DENGUE PATIENTS

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Nitric oxide, NO, is well accepted as one of the defense which inhibit viral dissemination. Macrophage and cell in macrophage lineage are professional nitric oxide producer which serves as target for dengue virus, DV. The interaction between NO and DV during natural infection is unknown. Therefore, the effect of NO on DV replication was investigated in vitro using s-nitroso-L-acetylpenicillamine, SNAP, as an exogenous nitric oxide donor. NO inhibited DV replication in a dose and MOI dependent manner that was NO from 50 and 75 μ M SNAP delayed and suppressed replication while higher concentration of NO, 100 μ M SNAP, completely